

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appln. of:

TAIT.

Application No. 10/762964

For: STOOL MARKER

DECLARATION BY KEVIN TAIT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Kevin Tait of Wahroonga, NSW, 2076, hereby declare:

1. I am the person named as inventor of the invention described in U.S. Application No. 10/762964. Considering the grounds of rejection set forth in the Office Action dated October 28, 2008, I provide the following.
2. The Examiner has stated that the polyacrylamide used in Queuille, US Patent 4,120,946 is used as a flocculant, despite the fact that Queuille describes it's function to be a thickening agent. With respect, the Examiner is incorrect. Queuille states that his preferred materials should be non-ionic. In order to be an efficient flocculant, a charged species, either cationic or anionic, needs to be present. I do not believe that anyone looking to encourage flocculation of barium sulfate particles would consider using a non-ionic polyacrylamide. In my view, Queuille's claim that the polyacrylamides must be non-ionic is clear evidence that he did not intend them to act as flocculants, but rather to be chemically benign.
3. In order to demonstrate that Queuille does not provide a flocculating composition, I have conducted a number of flocculation resistance tests using three formulations broadly along the lines of Example 1 as disclosed in Queuille, which I detail below, and compared the results against those obtained using my claimed formulation. The flocculation test is as described in my patent application and which forms part of my Claim 1. The tests in the present case all involved taking an amount of the formula equivalent to 0.25 g of barium sulfate diluted to 50

mL water. That is then titrated with a solution of 3.0% w/v ferrous sulfate which has been acidified with the dilute sulphuric acid to a pH of 5.0-5.5. The number of mL of titrant required before the suspension became coagulated was measured and recorded. The higher the number, the greater was the sample's resistance to flocculation by ionic species. The flocculation resistance is thus conveniently expressed in terms of mL titrant required.

4. None of the polyacrylamide materials specifically cited by Queuille appear to be currently available, however, I have used my best endeavours to prepare a range of test formulas in accordance with Queuille.
5. Test formula 1 was a sample of Roussel-Uclaf colloidal barium sulfate. A brochure for this is attached. It is my belief that the Roussel-Uclaf formula is that described in Queuille. Queuille, in US Patent 4,120,946 refers to his earlier US Patent 3,733,400, which was assigned to Roussel-Uclaf. It is my belief that the Queuille technology was commercialised by Roussel-Uclaf. All the claims of Queuille refer to "colloidal" barium sulfate. Roussel-Uclaf marketed a product that they described as "colloidal" barium sulfate from at least the early 1980's. As far as I am aware, no other barium sulfate supplier ever described their barium sulfate as "colloidal". The specification in the Roussel-Uclaf brochure accompanying this product is not very helpful. It states the composition has a >90% barium sulfate content, but mentions no additives. However, additives must be present, because the minimum purity allowed in pharmaceutical grade barium sulfate is 97.5%. Pure barium sulfate also has negligible acid extractable material, whereas the Roussel-Uclaf material allowed up to 3.5% w/w. Thus, the specification declared by Roussel-Uclaf is entirely consistent with the formula in Queuille provided at Example 1. Therefore, in my opinion, the flocculation resistance of the Roussel-Uclaf product is highly likely to represent that of US Patent 4,120,946. However, in any event, it represents a conventional imaging formula intended to be used in a conventional way, ie to coat the GIT, as stated in the brochure that accompanies it.
6. I have measured the flocculation resistance of this formulation using my test method and it currently tests at >30mL.
7. Test formula 2 was a formula made up using a generic polyacrylamide in accordance with US Patent 4,120,946 (non-ionic and >1 million MW), and using a grade of barium sulfate complying with normal pharmaceutical specifications. That is, it was made up as follows:

<u>Ingredient</u>	<u>Composition (% by weight)</u>
Barium Sulfate	58.3
Hydroxy-ethylcellulose	0.2
Glycerine	8.3
Food grade silicone	0.4
tromethamine	1.0
Citric acid	0.8
Polyacrylamide	0.6
methylparahydroxybenzoate	0.05
Water	30.35

8. I have measured this using my test method and it has a flocculation resistance of 28 mL.
9. Test formula 3 is a formula made up in accordance with US Patent 4,120,946 using a generic polyacrylamide that complies with Queuille's claim (non-ionic and >1 million MW), and using a grade of barium sulfate (Roussel-Uclaf colloidal barium sulfate) that would be classified as "colloidal" <1.0 μm mean diameter). That is, it was made up as follows:

<u>Ingredient</u>	<u>Composition (% by weight)</u>
Colloidal Barium Sulfate	58.3
Hydroxy-ethylcellulose	0.2
Glycerine	8.3
Food grade silicone	0.4
tromethamine	1.0
Citric acid	0.8
Polyacrylamide	0.6
methylparahydroxybenzoate	0.05
Water	30.35

10. I have measured this using my test method and it has a flocculation resistance of > 50 mL.

11. Test formula 4 is as disclosed in my patent application.

<u>Ingredient</u>	<u>Composition (% by weight)</u>
Barium Sulfate	95%
Smectite Clay	2.0%
Xanthan Gum	1.5%
Sodium Citrate	0.1%
Flavour, Sweetener, Preservatives	q.s.

12. I have measured this using my test method and it has a flocculation resistance of < 5ml

13. I also list below the flocculation resistance (abbreviated to F.R.) results that I have measured for a range of commercially available barium sulfate X-ray imaging agents that have at some time been marketed in the USA.

<u>Manufacturer</u>	<u>Tradename</u>	<u>Description</u>	<u>F.R. (mL)</u>
Covidien Ltd	Scan C	Barium sulfate suspension, 2.1% w/w	> 50 mL
Lafayette Pharmaceuticals	Medescan 1.2%	Barium sulfate suspension, 1.2% w/w	30 mL
E-Z-Em, Inc	Polibar ACB	Barium sulfate powder , 96% w/w	25 mL

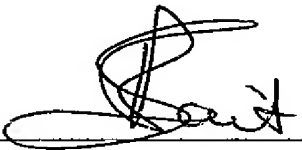
14. Test formula 1, 2 and 3 and three typical prior art x-ray imaging agents thus have flocculation resistances significantly different from my formulation, formula 4, and which are significantly outside the range of my claimed formulations. It is not difficult for a skilled person to change the flocculation resistance, but it is very unusual to have a low flocculation. As far as I am aware, until my invention, it has always been desirable to have high flocculation resistances.

15. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

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States Code, and that such willful false statements so made may jeopardize the validity of the document, or application, or any patent issuing thereon.

Date: 31 March 2009



Kevin Tait